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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/600,493	07/18/2000	Jack Wands	MGH-0026	3498

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/600,493	Applicant(s) WANDS ET AL.	
	Examiner Ram R. Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,6,11-28 and 32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,6,11-28 and 32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The after-final amendment and response filed 1-24-03 have been received and entered. The finality of the previous office action of 9-24-02 has been withdrawn in view of the newly discovered reference(s) and new grounds of rejections.

2. Claims 3, 4, 6, 11-28, and 32-46 are under consideration.

3. The enablement rejection of claims 3, 4 and 6-8 has been withdrawn in view of applicants' arguments.

4. Claims 18-28 and 34 are objected to because their dependence on the respective independent claims is not proper. It is noted that this has arisen due to the renumbering of the claims in the office action of 8-2-01. For the response to this office action to be fully responsive, applicants are required to correct the dependency of the claims and provide a list of all the claims properly depending on appropriate claims.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 11-16, 32, 33 and 39-46 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the previous office actions of 8-2-01, 3-28-02 and 9-24-02.

Response to Arguments

Applicant's arguments filed 1-24-03 have been fully considered but they are not persuasive to obviate all the rejections. As noted above the rejection of claims

3, 4, and 6-8 has been withdrawn in view of applicants' arguments, however, the rejection of the pharmaceutical compositions comprising the nucleic acids is maintained for reasons of record because of the intended use of the composition, i.e. treatment. Accordingly, only those arguments will be addressed that pertain to a pharmaceutical composition or treatment method. Applicants have argued that examiner has not provided evidence sufficient to doubt the truth of the disclosure stating that the claimed compositions and methods produce a sufficient immune response. Applicants are reminded that the examiner has provided scientific rationale supported by review by artisan in the field in the enablement rejection. Applicants have provided a declaration by the Dr. Wands, one of the co-inventors and in view of the declaration the enablement rejection of several claims has been withdrawn. However, the declaration of Dr. Wand does not obviate the rejection pertaining to a pharmaceutical composition and a method of treatment. The declaration does not provide any factual evidence to support the enablement of treatment or pharmaceutical composition claims. It is noted that while the article by Tokushige et al or Encke et al support producing immune response they do not provide any support for treatment. Again paragraphs 12 and 13 do not present any factual evidence. Regarding the issue of why the mouse model can not be extrapolated to human, applicants attention is directed to the office action of 8-2-01 which discusses the unpredictability of the art (eg. Houghton, Encke, and Chattergoon) and the discussion in the previous office action of 9-24-02. Applicants have not provided any new evidence to support their arguments.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for

> purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 3, 4, 6, 8, 11-13, 34, 36, 38, 39-41 and 45-46 are rejected under 35 U.S.C. 102(e) as being anticipated by Maertens et al (US 6,180,768 B1, 1-30-01, effective filing date 1995).

Maertens et al teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see claims 8-10). The vector comprises control elements for expression in eukaryotic cells. The specification discloses these control elements in columns 21-23. Accordingly, the claimed invention is anticipated by Maertens et al.

It is noted that the art is applicable to the pharmaceutical composition to the extent it reads on a composition.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 3, 4, 6-8, 11-28 and 34-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maertens et al (US 6,180,768 B1, 1-30-01, effective filing date 1995) or Selby et al (J. Gen.Virol. 74:1103-1113, 1993) in view of Tokushige et al Hepatology 24:14-20, 1996) and Ferrari et al (Hepatology 19:286-295).

Maertens et al teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see claims 8-10). The vector comprises control elements for expression in eukaryotic cells. The specification discloses these control elements in columns 21-23. Accordingly, the claimed invention is anticipated by Maertens et al. This art does not teach a method of producing an immune response in an animals by administering a nucleic acid comprising a nucleic acid encoding a hepatitis C virus nonstructural protein or combination.

Selby et al teaches several constructs for expression of viral proteins. For example, the plasmid pHCV comprises the entire viral genome (see the methods section on page 1103, right column continued into the left column on page 1104 and figure 1). The plasmids pHCV5-1 and pHCV comprise the entire 5'UTR and 3'UTR and the coding sequence for the non-structural proteins. Since the protein of the virus is produced as a polyprotein, a fusion of NS4-NS5 would be produced as a result of partial proteolytic digestion.

Tokushige et al teaches a method of producing immune response to hepatitis c virus core protein using a DNA based vaccine construct. The construct comprises a CMV promoter, an RSV enhancer, 5' UTR of hepatitis c virus and the coding sequence for core protein. The art also teaches method of injecting the construct in a muscle and using bupivacaine (see the materials and methods section).

Ferrari et al teach T cell response to structural and non-structural hepatitis c virus antigens in persistent and self-limited hepatitis c virus infections. The art teaches that the core protein followed by the NS4 were the most potent T-cell immunogen for both chronic as well as asymptomatic anti-HCV-positive patients . The art also teaches that another paper taught that NS4 was the most immunogenic. The art also discusses role of other non-structural protein NS5.

Diepolder et al teach T cell response to the other non-structural hepatitis c protein N3 and note that TH0/TH1-like CD4T-lymphocyte response to NS3 and other nonstructural HCV proteins contributes to successful viral clearance, whereas the PBMC response to core protein may be more common in patients that develop chronic hepatitis C. They go on to suggest that NS3-specific CD4 T-cell response might be a candidate as a target for immunointervention in the treatment of acute, protracted and chronic hepatitis and for vaccine development.

At the time of the invention, it would have been obvious to an artisan of ordinary skill to modify the polynucleotides of Maertens et al Selby et al by cloning the non-structural protein encoding sequences in the vector of Tokushige et al and administer them to an animal and produce immune response with a reasonable expectation of success. An artisan of skill would have been motivated to produce immune response against the non-structural proteins because they were known in the art to be strongly immunogenic and the art of record suggested their potential use in developing vaccine and treatment.

11. No claim is allowed.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this

application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

RAM R. SHUKLA, PH.D
PATENT EXAMINER

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632